Commissioner of Patents
USSN 10/661,402

REMARKS

Claims 52-56 are pending in the application. Claims 1-51 and 57 have been withdrawn.

Claim rejections - 35 U.S.C. § 112

Claims 52-56 have been rejected under 35 U.S.C. § 112, first paragraph. The Examiner states that the phrase "different from" in claim 52 renders the claim indefinite. Applicants respectfully point out that claim 52 has been amended to define that the antiviral oligonucleotide for use as an anti-viral agent against a target virus is not targeting HIV-1, HIV-2, HSV-1, HSV-2, CMV, RSV, parainfluenza virus, and HBV. Thus, any other virus different from HIV-1, HIV-2, HSV-1, HSV-2, CMV, RSV, parainfluenza virus, influenza virus and HBV is encompassed as being targeted by the antiviral oligonucleotide claimed in the present application. In view of the arguments and amendments presented hereinabove, reconsideration of the Examiner's rejection is respectfully requested.

Claims 52-56 have been rejected under 35 U.S.C. § 112, first paragraph. The Examiner states that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. Further, the Examiner alleges that the description would need to describe a representative oligonucleotide against many viral families. In order to overcome this rejection, Applicants respectfully point out to the Examiner that it is mentioned in the Manual of Patent Examining Procedure that:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species. A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure "indicates that the patentee has

invented species sufficient to constitute the genus" (Manual of Patent Examining Procedure 2163.05).

Applicants further point out that in the application, as acknowledged by the Examiner, results are disclosed demonstrating the antiviral activity of the antiviral oligonucleotides claimed in the present application against HIV-1, HIV-2, HSV-1, HIV-2, RSV, parainfluenza virus and HBV and against other viruses from four different families, namely Coxsackie virus B2 (*Picornaviridae*, RNA virus), vaccinia virus (*Poxviridae*, DNA virus) , hantavirus (*Bunyaviridae*, RNA virus) and parainfluenza-3 virus (*Paramyxoviridae*, RNA virus). Results disclosed in the application are believed to be predictive of the activity of the claimed oligonucleotides against other families of viruses. To support this latter allegation, enclosed is a Declaration of Dr. Jean-Marc Juteau, one of the inventors, reporting *in vitro* and *in vivo* assays demonstrating the antiviral activity of the oligonucleotides claimed in the present application, covering different viruses, i.e. different viral families, different strains, RNA and DNA viruses. Thus, the antiviral activity of the sequence independent oligonucleotides claimed in the present application has been demonstrated in a "representative number of species", being 28 different viruses from 13 families, in the application and in the Declaration presented hereinabove. Consequently, it is believed that Applicants have described sufficient variety of species to reflect the variation within the genus. In view of the foregoing, reconsideration and withdrawal of the Examiner's rejection of claims 52-56 under 35 U.S.C. § 112, first paragraph, are respectfully requested.

Claims 52-56 have been rejected under 35 U.S.C. § 112, first paragraph. The Examiner states that the specification, while enabling for an antiviral oligonucleotide against HIV, HSV, CMV and RSV, does not reasonably provide enablement for an antiviral oligonucleotide against every virus that causes infection. The specification does not enable any person skilled in the art to which it pertains to make the specific antiviral oligonucleotides of the invention commensurate in scope with the claims. In order to overcome this rejection, Applicants respectfully submit that results are disclosed in the present application demonstrating the antiviral activity of the antiviral oligonucleotides claimed in the present application against HIV-1, HIV-2, HSV-1, HIV-2, RSV, parainfluenza virus and HBV and against other viruses from four different families, namely Coxsackie virus B2, vaccinia virus, hantavirus and parainfluenza-3 virus. In addition, results are also

disclosed in the Declaration of Dr. Jean-Marc Juteau, as mentioned hereinabove, reporting *in vitro* and *in vivo* assays demonstrating the antiviral activity of the oligonucleotides claimed in the present application, covering different viruses, i.e. different viral families, different strains, RNA and DNA viruses. Thus, the antiviral activity of the sequence independent oligonucleotides claimed in the present application has been demonstrated against 28 different viruses from 13 families. Consequently, there is sufficient evidence that a skilled artisan can predict the operability of the antiviral activity of the oligonucleotides claimed in the present application against any species of viruses. One of ordinary skill in the art following the teaching disclosed in the present application would be able to make oligonucleotides with antiviral activity against any viruses. In view of the foregoing, reconsideration and withdrawal of the Examiner's rejection of claims 52-56 under 35 U.S.C. § 112, first paragraph, are respectfully requested.

Claim rejections - 35 U.S.C. § 102

Claims 52-56 have been rejected under 35 U.S.C. § 102(e) as being anticipated by Peyman *et al.* (US Patent No. 6,013,639). The Examiner states that Peyman *et al.* teaches a method for the preparation of modified oligonucleotides, having a length of 6 to 60 nucleotides, with phosphorothioate bridges and that these oligonucleotides can be linked to molecules. Further, Peyman *et al.* teaches a process for preparing pharmaceutical compounds or therapeutically effective oligonucleotides which may be used for treating diseases, which are caused by viruses, for example, HIV, HSV-1, HSV-2, influenza, VSV, hepatitis B or papilloma viruses. In order to overcome this rejection, Applicants first point out that claim 52 has been amended to define that the anti-viral activity of said oligonucleotide occurs principally by a non-sequence complementary mode of action. Support can be found on page 11 of the present specification. In addition, Applicants respectfully point out that, contrary to the teaching of the present application, Peyman *et al.* teaches that the efficacy of the tested oligonucleotides is dependent on the presence of a 10 guanines extension at each extremity of the oligonucleotides. It is clearly stated in Peyman *et al.* (column 1 and 2, under the Summary section), that:

> *"It has now been found that a very simple option exists for significantly improving unmodified or modified oligonucleotides with regards to their nuclease resistance and cell penetration, so that their activity is substantially*

improved, by extending the oligonucleotides at the 3' end and/or 5' end by from one to 10 guanines.

Surprisingly, the novel oligonucleotide also exhibits a tendency to associate or aggregate. It is possible that they too form G quartet structures by the association of two or more oligonucleotide. Such structures would protect against exonuclease degradation and lead to an increased uptake in cell."(emphasis added)

These oligonucleotides adopt a « G quartet » structure, which is not required in the present invention. The present application neither claims nor teaches that the efficacy of the oligonucleotides claimed is dependent on the presence of a 10 guanines extension at each extremity of the oligonucleotides. On the contrary, there is no such constraint in the sequence of the oligonucleotides claimed in the presence invention. Furthermore, Peyman *et al.* never recognized oligonucleotides having an antiviral activity, wherein said activity occurs with a non-sequence complementary mode of action (with at least one phosphorothioate linkage). In Peyman *et al.*, the modified oligonucleotides need to be directed to a specific target to exhibit activity. The specification of Peyman *et al.* is replete with examples of antisense oligonucleotides that are directed to specific targets. See column 6, lines 11-12 and 30-31, column 7, lines 25-28, column 8, lines 29-30, column 10, lines 35-36, column 11, lines 4-5 and column 14, lines 14-15, among others. In fact, Peyman *et al.* only provides for the teaching of modified oligonucleotides for improving nuclease resistance and cell penetration. Peyman *et al.* suggests that the modified oligonucleotides have activity, such as antiviral activity, only if such oligonucleotides target specific viral targets through an antisense mechanism - with a sequence dependent mode of action. Again, nowhere does Peyman *et al.* recognize a non-sequence complementary mode of action of oligonucleotides with at least one phosphorothioate linkage. In view of the arguments submitted hereinabove, reconsideration of the Examiner's rejections is respectfully requested.

Double Patenting

Claims 52-56 have been provisionally rejected under 35 U.S.C. § 101 and on the grounds of double patenting as being unpatentable over claims 53-57 of co-pending Application No. 10/969,812. In order to overcome this rejection, Applicants respectfully

point out that claim 52 has been amended to encompass a method for selecting an antiviral oligonucleotide for use as an anti-viral agent against a target virus and not targeting HIV-1, HIV-2, HSV-1, HSV-2, CMV, RSV, parainfluenza virus, influenza virus, and HBV. Support can be found on page 94 of the present description. In addition, Applicants will consequently restrict the corresponding claim in co-pending Application No. 10/969,812 to encompass a method for selecting an antiviral oligonucleotide for use as an anti-viral agent against the influenza virus. In view of the amendments and arguments submitted hereinabove, reconsideration of the Examiner's rejections is respectfully requested.

It is submitted, therefore, that the claims are now in condition for allowance. Reconsideration of the Examiner's rejections is respectfully requested. Allowance of claims 52-56 at an early date is solicited.

No additional fees are believed to be necessitated by this amendment. Should this be in error, authorization is hereby given to charge Deposit Account No. 19-5113 for any underpayment or to credit any overpayment.

In the event that there are any questions concerning this amendment or the application in general, the Examiner is respectfully urged to telephone the undersigned so that prosecution of this application can be expedited.

Respectfully,

Date: September 8, 2006

By: 

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Enc. Declaration of Jean-Marc Juteau